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REMARKS

Prior to this response, claims 1 to 8 were pending and under examination. In the present communication, claim 1 has been amended to define Applicant's invention with greater particularity as shown in attached Exhibit A, and claims 10 to 56 have been cancelled without prejudice. No new matter is added by the amendments, the amended claim language being fully supported by the Specification and original claims. Applicant submits that the claim amendments do not narrow the claims in any way within the meaning of Festo Corporation v. Shoketsu Kinzoku Kogyo Kabushiki Co. Ltd., a/k/a SMC Corporation and SMC Pneumatics, Inc. 234 F.3d 558, 51 U.S.P.Q. 2d 1959 (Fed. Cir. 2000). Accordingly claims 1-8 are currently pending.

Objections to Claims

In response to the objection of claims 4 to 8 because claims 4 to 8 depend from rejected claims 1 and 3, it is respectfully submitted that amendment to claim 1 places the claim in condition for allowance. Thus, claims 4 to 8 may properly depend on claim 1. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the objection.

Rejection Under 35 U.S.C. § 102(b)

The rejection of claims 1, 2 and 3 under 35 U.S.C. § 102(e) as being allegedly anticipated by Tsien *et al.* (United States Patent Number 5,981,200; hereinafter "Tsien") is respectfully traversed. Applicants' invention, defined by amended claim 1, distinguishes over Tsien by requiring a fusion protein comprising a reporter polypeptide selected from an enzyme, a transcriptional activator, and an antibody or active fragment thereof, such as a single chain antibody, linked to a linker polypeptide comprising a protease cleavage site and a repressor polypeptide that represses the activity of said reporter polypeptide. The repressor polypeptide is operatively linked to the reporter polypeptide by a linker polypeptide containing a protease cleavage site, wherein

cleavage of the linker polypeptide at the protease cleavage site increases the activity of said reporter.

In contrast, Tsien is absolutely silent regarding such a fusion protein. For example, Tsien is silent regarding a fusion protein comprising an enzyme, a transcriptional activator or an antibody or active fragment thereof as a reporter polypeptide. Instead Tsien discloses a tandem fluorescent protein construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety, and a peptide linker that couples the donor and acceptor fluorescent protein moieties. Tsien teaches only fluorescent protein moiety constructs containing two fluorescent protein moieties. Thus, Tsien does not teach or suggest using protein constructs containing a repressor protein and a reporter protein. Therefore, Tsien fails to disclose each and every element of Applicants' invention defined by amended claim 1, as would be required to support a rejection for anticipation under 35 U.S.C. § 102(e). Accordingly Applicant respectfully requests reconsideration and withdrawal of the rejection over Tsien under 35 U.S.C. § 102 (e).

Applicant also traverses the rejection of claims 1 and 3 under 35 U.S.C. § 102(b) as allegedly being anticipated by Knight *et al.* (*Methods in Enzymology*, (1995) 248:18-34; hereinafter "Knight"). is respectfully traversed.

Applicants' invention, as defined by amended claim 1, distinguishes over Knight by requiring a fusion protein comprising a reporter polypeptide linked to a linker polypeptide and a repressor polypeptide that represses the activity of the reporter polypeptide. Upon cleavage of the linker polypeptide at a protease cleavage site, activity of the reporter polypeptide is increased. The reporter polypeptide is selected from an enzyme, a transcriptional activator and an antibody or active fragment thereof.

Knight is absolutely silent regarding fusion protein as described by claim 1. For example, Knight is silent regarding a fusion protein comprising a reporter polypeptide selected from an enzyme, a transcriptional activator and an antibody or active fragment. Instead, Knight

teaches constructs of fluorescent proteins and as acknowledged by the Examiner in the Office Action mailed December 5, 2001 (Paper No. 8), Knight discloses constructs that employ resonance energy transfer rather than a "repressor" that upon cleavage of the linker moiety allows an increase in activity of the reporter polypeptide. Indeed, Knight does not teach or suggest a construct comprising any non-fluorescent protein moiety.

Therefore, Applicant respectfully submits that Knight fails to disclose each and every element of Applicants' invention defined by amended claim 1, as would be required to support a rejection for anticipation under 35 U.S.C. § 102(b). Accordingly reconsideration and withdrawal of the rejection over Knight under 35 U.S.C. § 102 (b) are respectfully requested.

In view of the above amendments and remarks, reconsideration and favorable action on all pending claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is requested to telephone Lisa A. Haile, J.D., Ph.D., at (858) 677-1456 or the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: April 2, 2002

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Enclosure: Exhibit A

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EXHIBIT A

A Marked-Up version of the amendments

In the Claims

Please cancel without prejudice claims 10 to 56.

Please amend claim 1 as follows:

1. (Amended) A fusion protein comprising:

b) a reporter polypeptide linked to a linker polypeptide comprising a protease cleavage site;

wherein said reporter polypeptide is an enzyme, a transcriptional activator, or [a polypeptide having at least one epitope] an antibody or active fragment thereof; and

b) a repressor polypeptide that represses the activity of said reporter polypeptide, wherein said repressor polypeptide is operatively linked to the linker polypeptide, and

wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter.